

**Amendments to the Specification:**

At page 8, lines 22-28:

Figure 9. Structure and sequence of mouse and human OPG cDNA clones. A, B. Mouse cDNA and protein sequence. C, D. Human cDNA and protein sequence. The predicted signal peptides are underlined, and potential sites of N-linked glycosylation are indicated in bold. E, F. Sequence alignment and comparison of rat, mouse and human OPG amino acid sequences. Muosteo (SEQ ID NO: [[171]]123); ratosteo (SEQ ID NO: [[172]]121); huosteo (SEQ ID NO: [[173]]125).

At page 14, lines 13-17:

Figures 31A and 31B. Combination treatment with OPG-Fc and ~~sTNFR-IsTNFR-I~~ on Adjuvant Arthritis in Male Lewis Rats. Area under the curve (AUC) for measurement of paw swelling and BMD were measured as described above for Figure 33 and in the examples hereinafter.

At page 69, lines 1-27:

**Pharmaceutical compositions**

The invention also provides for pharmaceutical compositions comprising a therapeutically effective amount of a polypeptide comprising OPG or the other therapeutic molecules used (e.g., IL-1ra, ~~sTNFR-IsTNFR-I~~, or SLPI) together with a pharmaceutically acceptable diluent, carrier, solubilizer, emulsifier, preservative and/or adjuvant. Two or more of the therapeutic molecules (e.g., OPG, IL-1ra, ~~sTNFR-IsTNFR-I~~, or SLPI) can be formulated together or packaged together in a kit. The term "therapeutically effective amount" means an amount which provides a therapeutic effect for a specified condition and route of administration. The composition may be in a liquid or lyophilized form and comprises a diluent (Tris, acetate or phosphate buffers) having various pH values and ionic strengths, solubilizer such as Tween or Polysorbate, carriers such as human serum albumin or gelatin, preservatives such as thimerosal or benzyl alcohol, and antioxidants such as ascorbic acid or sodium metabisulfite. Also encompassed are compositions comprising any of the therapeutic molecules modified with water-soluble polymers to increase solubility or stability. Compositions may also comprise incorporation of any of the therapeutic molecules into liposomes, microemulsions, micelles or vesicles for controlled delivery over an extended period of time.

At page 75, lines 14-23:

- TNF- $\alpha$  inhibitors: soluble tumor necrosis factor receptor type I (~~sTNFR-IsTNFR-I~~; -RI is also called the p55 receptor); soluble tumor necrosis factor receptor type II (also called the p75 receptor); and monoclonal antibodies that bind the TNF receptor. Most preferred is ~~sTNFR-IsTNFR-I~~ as described in WO 98/24463,

etanercept (Enbrel®), and Avakine®. Exemplary TNF- $\alpha$  inhibitors are described in EP 422 339, EP 308 378, EP 393 438, EP 398 327, and EP 418 014.

At page 173, lines 8-25:

To study the effects of OPG-Fc on BMD in adjuvant arthritis, paws from two experiments were analyzed by DEXA. The results of BMD measurements on the tibiotarsal region are shown in ~~Figures 2 and 4~~ Figures 30A and 30B. Bone protective effects were observed in rats with adjuvant-arthritis treated with OPG-Fc via subcutaneous daily injection (from day 9 to day 15 after mycobacteria injection). Treatment with OPG-Fc at 4, 1, 0.25, 0.06, .016, and 0.004 mg/kg showed 100%, 100%, 100%, 86%, 22, and 22% inhibition of bone mineral density loss respectively. Treatment of the intermediate and high doses of OPG-Fc (4 – 0.06 mg/kg) showed a statistically significant difference in BMD when compared to the OPG placebo treated control group ( $P < 0.05$ ).

However, treatment with OPG-Fc (at all doses) had no statistically significant effect on the severity of inflammation (Figure 1 and 3, AUC) or loss of body weight (data on file).

At page 174, lines 33-34:

Combination treatment with OPG-Fc and sTNFR-I sTNFR-I on Adjuvant Arthritis in Male Lewis Rats

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 - 16 (Canceled).

17. (Currently amended) A method of treating a condition resulting in bone loss, which comprises administering an IL-1 inhibitor, a TNF- $\alpha$  inhibitor, and an OPG protein, wherein "OPG protein" refers to an antibody to OPG ligand or a polypeptide comprising conserved residues from residues 22 to 185 of SEQ ID NOS: ~~171, 172, and 173~~ 121, 123, and 125.
18. (Original). The method of Claim 17, wherein the TNF- $\alpha$  inhibitor comprises sTNFR-I, sTNFR-II, sTNFR fragments, or sTNFR-Fc, wherein "sTNFR" refers to sTNFR-I or sTNFR-II.
19. (Previously amended) The method of Claim 17, wherein the TNF- $\alpha$  inhibitor comprises sTNFR-I, sTNFR-II, sTNFR fragments, or sTNFR-Fc, wherein "sTNFR" refers to sTNFR-I or sTNFR-II.
20. (Original). The method of claim 17, wherein the TNF- $\alpha$  inhibitor comprises 30 kD PEG-sTNFR-I.
21. (Currently amended). The method of claim ~~18~~ 17, wherein the ~~sTNFR-I~~ sTNFR fragment is a 2.6 kD sTNFR-I fragment.
22. (Currently amended). The method of claim 21, wherein the ~~sTNFR-I~~ sTNFR-I fragment comprises 30 kD PEG.
23. (Original). The method of claim 17, wherein the TNF- $\alpha$  inhibitor comprises sTNFR-II linked to an Fc region.
24. (Original). The method of claim 17, wherein the TNF- $\alpha$  inhibitor is etanercept.
25. (Original). The method of Claim 17, wherein the OPG protein is OPG-Fc.

Claim 26-38 (Canceled).

- 39. (Previously amended) The method of any of claims 17 to 25, wherein the condition treated is rheumatoid arthritis.
- 40. (Previously amended) The method of any of claims 17 to 25, wherein the condition treated is multiple sclerosis.
- 41. (Previously amended) The method of any of claims 17 to 25, wherein the condition treated is osteoporosis.
- 42. (Previously amended) The method of any of claims 17 to 25, wherein the condition treated is osteomyelitis.

Claim 43 - 61 (Canceled).

- 62. (Previously added) The method of Claim 17, wherein the OPG protein comprises a sequence comprising the conserved residues from residues 22 to 185 of SEQ ID NOS: 171, 172, and 173.
- 63. (Previously added) The method of Claim 17, wherein the OPG protein comprises residues 22 to 185 of SEQ ID NO: 123.
- 64. (Previously added) The method of Claim 17, wherein the OPG protein comprises residues 22 to 185 of SEQ ID NO: 125.
- 65. (Previously added) The method of Claim 17, wherein the OPG protein comprises an antibody to OPG ligand.
- 66. (New) The method of Claim 17, wherein the TNF- $\alpha$  inhibitor is etanercept.

**Amendment to the Sequence:**

The attached paper copy and computer readable form (CRF) of the "Sequence Listing" replaces the previously submitted Sequence Listing.

Attachment: Attorney Statement, Sequence Listing and CRF.